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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/814,232

04/01/2004

Kei Takenaka

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EXAMINER

BOWERS, NATHAN ANDREW

ART UNIT

PAPER NUMBER

1797

MAIL DATE

DELIVERY MODE

05/09/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/814,232

Applicant(s)

TAKENAKA ET AL.

Examiner

NATHAN A. BOWERS

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/CDC)
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(c), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(c) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11 March 2008 has been entered.

Claim Rejections - 35 USC § 112

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The independent claims do not clearly indicate that the second heating mechanism is comprised of eight separate heating zones, such that each of the heating zones interacts with a separate branch flow passage. The current wording of claims 1 and 3 suggests that a unitary second heating element is used to produce eight different temperature zones along the unitary second heating element body. The claims must more clearly reflect the invention disclosed in the specification and the drawings – the use of eight different heating elements each set at a different temperature between 55 and 62 degrees Celsius.

Claims 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP

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§ 2172.01. The independent claims do not clearly indicate that the second set temperatures are provided by using eight separate heating zones that each interact with a separate branch flow passage. The current wording of claims 9 and 10 fails to indicate that the gradient is formed using a plurality of heating elements each set at a different temperature. The claims must more clearly reflect the invention disclosed in the specification and the drawings – the use of eight different heating elements each set at a different temperature between 55 and 62 degrees Celsius.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1, 7 and 8 rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen (US 6180372) in view of Schulte (US 20010046701).

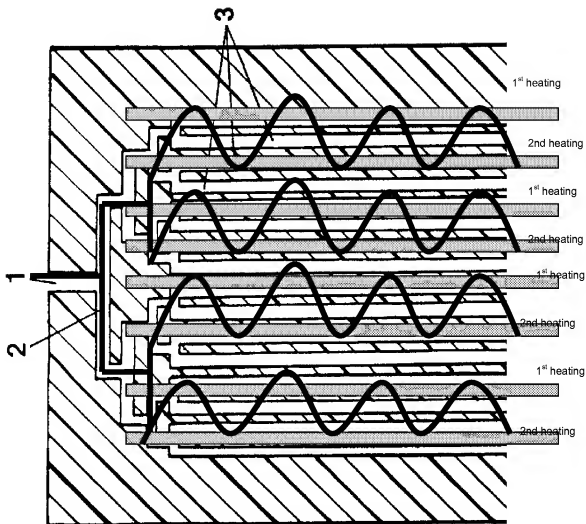
With respect to claims 1 and 7, Franzen discloses a nucleic acid amplifying apparatus comprising a flow passage through which a reaction fluid containing a nucleic acid and a reagent flows. The flow passage includes a flow passage branch portion (Figure 2:2) at which the flow passage branches into a plurality of branch flow passages (Figure 2:3). A junction portion (Figure 2:4) is also provided at which the plurality of flow passages join. This is described in column 8, line 29 to column 9, line 2. Column 6, lines 30-52 state that a heating mechanism is provided to cycle the fluid moving through the branch flow passages through a plurality of different temperatures. Franzen, however, teaches that a heating element is used to produce different temperatures over time. Franzen does not expressly disclose a plurality of set temperature zones provided by a first and second heating mechanism.

Schulte discloses a thermal cycling device capable of amplifying nucleic acid samples via PCR. Paragraph [0025] indicates that a flow passage (Figure 2:12) is provided such that fluids are repeatedly passed through a plurality of zones and heated by different heating mechanisms. Heating elements (Figure 2:14,16) can be held at 95 degrees Celsius and cooling elements (Figure 2:18,20) can be held between 45 and 50 degrees Celsius.

Franzen and Schulte are analogous art because they are from the same field of endeavor regarding thermal cycling apparatuses.

At the time of the invention, it would have been obvious to replace the programmable heating mechanisms of Franzen with a plurality of heating elements maintained at a set temperature. In Figure 2, Schulte teaches that it is known in the microfluidic thermal cycling art to repeatedly move fluids across several heating areas in order to produce a temperature change in the nucleic acid solution. One of ordinary skill in the art would recognize that the use of first and second heating mechanisms maintained at steady temperatures would offer a viable and effective alternative to the use of a single heating mechanism that is cycled between two temperatures. Moving a nucleic acid sample repeatedly across a several set heating regions in order to affect temperature change in the fluid is considered to be well known in the art.

Upon review of the Schulte reference (and particularly Figure 2), one of ordinary skill in the art would have found it obvious to modify each of the branch portions of Franzen as follows:



Schulte, like the Fouillet reference cited in the previous rejection, does not expressly teach that the second heating mechanisms are provided each at a different temperature such that a temperature gradient is formed with each of the second temperatures zones being sequentially set at intervals of 1 degree Celsius between 55 and 62 degrees Celsius.

However, these limitations represent an intended use that is not given significant patentable weight when evaluating an apparatus claim. The temperature control systems disclosed by Franzen and Schulte are each fully capable of being reprogrammed or reconfigured

to ensure that the second heating mechanisms are maintained at different temperatures offset by 1 degree Celsius. There is nothing special about the Schulte heating elements that prohibits their use within the interval of 55 to 62 degrees Celsius. Independent claim 1 recites structural limitations pertaining to (1) a flow passage, (2) a branch portion, (3) a junction portion, (4) a joined passage, (5) a first heating mechanism and (6) a second heating mechanism. As noted in the rejections above, the Franzen reference discloses limitations (1)-(4), and the Schulte reference discloses limitations (5) and (6) through describing a flow passage arranged to repeatedly pass through first and second temperature zones. In this way, all of the structural limitations set forth in independent apparatus claim 1 are found in the cited prior art. Although Franzen and Schulte do not teach that a temperature gradient between 55 and 62 degrees Celsius is formed by varying each of the second heating mechanisms by 1 degree Celsius, the combined device of Franzen and Schulte is capable of being used according to this intended use.

In response to applicant's argument that the prior art does not disclose a plurality of second heating mechanisms each maintained at varying temperatures between 55 and 62 degrees Celsius, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

With respect to claim 8, Franzen and Schulte disclose the combination as previously described above. In addition, Schulte indicates in paragraphs [0026], [0027] and [0031]-[0034] that it is known to provide microfluidic thermal cycling devices with an integrated detection

system capable of detecting a desired product. At the time of the invention, it would have been obvious to ensure that the system of Franzen is provided with a detection part that detects the nucleic acid in the reaction fluid following and/or during thermal cycling. In this way, the use of additional, remote detection devices would no longer be necessary, which would improve the efficiency of the operation.

2) Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen (US 6180372) in view of Schulte (US 20010046701) and Bedingham (US 6720187).

Franzen and Schulte disclose the combination as previously described in the rejections above, however do not expressly disclose that the use of a second branch portion and second branch flow passages.

Bedingham discloses a microfluidic system in which a plurality of flow passages containing a nucleic acid solution are split in order to undergo thermal cycling within separate temperature regions (Figure 10:440). This is disclosed in column 20, line 42 to column 21, line 20. Following the initial thermal cycling, the fluid channels are branched for a second time, and the sample is subjected to a second heat treatment at individual heating areas (Figure 10:460).

Franzen, Schulte and Bedingham are analogous art because they are from the same field of endeavor regarding microfluidic thermal cycling devices.

At the time of the invention, it would have been obvious to alter the apparatus and method set forth by Franzen and Schulte in order to provide a second branch portion and second branch flow passages disposed downstream from the first branch portion and the first branch flow passages. Bedingham teaches that microfluidic devices comprising multiple branching

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steps are well known in art. The addition of a second branch portion to Franzen's device would have been beneficial because it would have allowed the sample solution to experience extra temperature cycles capable of enhancing nucleic acid amplification. Since Franzen already discloses the use of a branch portion and branch flow passages subjected to heating, the addition of a second branch portion and second branch flow passages merely represents the duplication of parts already disclosed in the prior art. It would have been apparent to add second, third, fourth, etc branch portions to the system of Franzen to obtain the expected result of additional thermal cycling area. See MPEP 2144.04.

Allowable Subject Matter

Claims 9-11 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

The prior art does not disclose, in the claimed environment, a nucleic acid amplifying method comprising the branching of a reaction fluid such that each branch encounters a separate first heater maintained at 95 degrees Celsius and a separate second heater, wherein each of the plurality of second heaters are maintained as a temperature gradient ranging from 55 to 62 degrees Celsius with eight temperature zones that are sequentially set at intervals of 1 degree Celsius. The Franzen reference represents the closest prior art in that it discloses a thermal cycling device that comprises a plurality of branched channels that each undergo heating and cooling. Franzen, however, does not disclose that each branch interacts with a second set temperature offset by 1 degree Celsius from the second set temperature of neighboring channels.

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The Schulte reference teaches that it is known in the art to repeatedly expose a channel to first and second set temperatures, but does not teach that a plurality of second set temperatures are provided in order to form a temperature gradient ranging from 55 to 62 degrees Celsius.

Response to Arguments

Applicant's arguments filed 11 March 2008 with respect to the 35 U.S.C. 102 rejections involving Franzen have been fully considered and are persuasive. These rejections have been withdrawn.

Applicant's arguments filed 11 March 2008 with respect to the 35 U.S.C. 103 rejections involving the combination of Franzen with Fouillet have been fully considered and are persuasive. Therefore, these rejections have been withdrawn. However, upon further consideration, a new ground of rejection is made in view of the combination of Franzen with Schulte and the combination of Franzen with Schulte and Bedingham.

Conclusion

This is a non-final rejection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner, Art Unit 1797

/Nathan A Bowers/
Examiner, Art Unit 1797